GAU 1641

Atty Dkt [redacted]3.002
Client No. 2302-1393
PATENT

#16

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on July 18, 2000.

7/18/00 Patricia K. Jones
Date Signature



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

BARCHFIELD et al.

Serial No.: 09/044,696 Group Art Unit: 1641

Filing Date: March 18, 1998 Examiner: S. Devi

Title: DETOXIFIED MUTANTS OF BACTERIAL ADP-RIBOSYLATING TOXINS AS PARENTERAL ADJUVANTS

**TRANSMITTAL LETTER**

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Transmitted herewith for filing is an Supplemental Information Disclosure Statement, including a Form PTO-1449 and copies of the cited references. It is believed that no fee is due.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16, 1.17 and 1.21 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 18-1648.

Respectfully submitted,

Date: 7/18/00 By: Roberta L. Robins

Roberta L. Robins
Registration No. 33,208
Attorney for Applicants

CHIRON CORPORATION
Intellectual Property-R440
P.O. Box 8097
Emeryville, CA 94662-8097
Telephone: 510-655-2708
Facsimile: 510-655-3542

Atty D[redacted]393.002
2302-1393
PATENT

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on July 18, 2000.

7/18/00
Date

Patricia K. Adams
Signature

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

BARCHFELD et al.

Serial No.: 09/044,696 Group Art Unit: 1641

Filing Date: March 18, 1998 Examiner: S. Devi

Title: DETOXIFIED MUTANTS OF BACTERIAL ADP-RIBOSYLATING TOXINS AS PARENTERAL ADJUVANTS

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

The information listed below may be material to the examination of the above-identified application. Copies of the information and completed PTO-1449 forms are submitted herewith. The Examiner is respectfully requested to make this information of official record in the application. The information includes:

International Publication No. WO 96/06627, published March 7, 1996;

European Patent Publication No. 0 145 486 A2 published June 19, 1985;

Burnette et al., "Site-Specific Mutagenesis of the Catalytic Subunit of Cholera Toxin: Substituting Lysine for Arginine 7 Causes Loss of Activity," *Infection and Immunity* 59(11):4266-4270 (1991);

Di Tommaso et al., "Induction of Antigen-Specific Antibodies in Vaginal Secretions by Using a Nontoxic Mutant of Heat-Labile Enterotoxin as a Mucosal Adjuvant," *Infection and Immunity* 64(3):974-979 (1996);

Douce et al., "Mutants of *Escherichia Coli* Heat-Labile Toxin Lacking ADP-Ribosyltransferase Activity Act as Nontoxic, Mucosal Adjuvants," *Proc. Natl. Acad. Sci. USA* 92:1644-1648 (1995);

Douce et al., "Intranasal Immunogenicity and Adjuvanticity of Site-Directed Mutant Derivatives of Cholera Toxin," *Infection and Immunity* 65(7):2821-2828 (1997);

Fontana et al., "Construction of Nontoxic Derivatives of Cholera Toxin and Characterization of the Immunological Response Against the A Subunit," *Infection and Immunity* 63(6):2356-2360 (1995);

Harford et al., "Inactivation of the *Escherichia Coli* Heat-Labile Enterotoxin by *In Vitro* Mutagenesis of the A-Subunit Gene," *Eur. J. Biochem.* 183:311-316 (1989);

Holmgren et al., "An Oral B Subunit: Whole Cell Vaccine Against Cholera," *Vaccine* 10(13):911-914 (1992);

Jackson et al., "Optimizing Oral Vaccines: Induction of Systemic and Mucosal B-Cell and Antibody Responses to Tetanus Toxoid by Use of Cholera Toxin as an Adjuvant," *Infection and Immunity* 61(10):4272-4279 (1993);

Magagnoli et al., "Mutations in the A Subunit Affect Yield, Stability, and Protease Sensitivity of Nontoxic Derivatives of Heat-Labile Enterotoxin," *Infection and Immunity* 64(12):5434-5438 (1996);

Nashar et al., "Potent Immunogenicity of the B Subunits of *Escherichia Coli* Heat-Labile Enterotoxin: Receptor Binding is Essential and Induces Differential Modulation of Lymphocyte Subsets," *Proc. Natl. Acad. Sci. USA* 93:226-230 (1996);

Partidos et al., "The Adjuvant Effect of a Non-Toxic Mutant of Heat-Labile Enterotoxin of *Escherichia Coli* for the Induction of Measles Virus-Specific CTL Responses After Intranasal Co-Immunization With a Synthetic Peptide," *Immunology* 89:483-487 (1996);

Pizza et al., "Probing the Structure-Activity Relationship of *Escherichia Coli* LT-A by Site-Directed Mutagenesis," *Molecular Microbiology* 14(1):51-60 (1994);

Rollwagen et al., "Killed *Campylobacter* Elicits Immune Response and Protection When Administered With an Oral Adjuvant," *Vaccine* 11(13): 1316-1320 (1993);

Tsuji et al., "A Single Amino Acid Substitution in the A Subunit of *Escherichia Coli* Enterotoxin Results in a Loss of Its Toxic Activity," *The Journal of Biological Chemistry* 265(36):22520-22525 (1990); and

van den Akker et al., "The Arg7Lys Mutant of Heat-Labile Enterotoxin Exhibits Great Flexibility of Active Site Loop 47-56of the A Subunit," *Biochemistry* 34:10996-11004 (1995).

This Supplemental Information Disclosure Statement under 37 CFR § 1.97 is not to be construed as a representation that: (i) a complete search has been made; (ii) additional information material to the examination of this application does not exist; (iii) the information, protocols, results and the like reported by third parties are accurate or enabling; or (iv) the above information constitutes prior art to the subject invention.

Respectfully submitted,

Date: 7/18/00

By: _____
Roberta L. Robins
Registration No. 33,208
Attorney for Applicants

CHIRON CORPORATION
Intellectual Property-R440
P.O. Box 8097
Emeryville, CA 94662-8097
Telephone: 510-655-2708
Facsimile: 510-655-3542